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NEW METHODS

Cardiac Index Quantification by Doppler Ultrasound in Patients Without Left Ventricular Outflow Tract Abnormalities

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Objectives. **We attempted to ascertain whether cardiac index can be directly estimated from Doppler mean velocity.**

Background. **Although diverse Doppler echocardiographic methods have been described for cardiac output quantification, they are not widely used in clinical practice. Cross-sectional area measurement has been identified as the main source of error in flow volume quantification.**

Methods. **A three-phase study by Doppler echocardiography was conducted in 306 patients. In phase I, the normal mean velocity ratio of the left and right ventricular outflow tracts was established in 170 normal subjects. In phase II, cardiac index, calculated as the product of aortic annular area index by mean velocity (conventional method), and mean velocity determined in the left ventricular outflow tract and ascending aorta by pulsed and continuous wave Doppler, respectively, were correlated with thermodilution cardiac index in 66 patients. In phase III, the accuracy of the regression equations obtained was prospectively assessed in an additional 70 patients.**

Results. **The normal left/right ventricular outflow tract mean velocity ratio by pulsed wave Doppler was 1.1 ± 0.1. Cardiac index (CI) calculated by the conventional method and thermodilution (TD) showed acceptable correlation (r = 0.90, $CI_{TD} = 1.20\ CI_{PWD} + 357$; r = 0.86, $CI_{TD} = 0.90\ CI_{CWD} + 262$) for pulsed (PWD) and continuous wave (CWD) Doppler, respectively, but with systematic underestimation (−28 ± 13%, p < 0.01) by pulsed wave Doppler. Mean velocity (MV) showed excellent correlation with the thermodilution cardiac index (r = 0.97, $CI_{TD} = 172\ MV_{PWD} - 172$; r = 0.93, $CI_{TD} = 129\ MV_{CWD} - 255$). When these regression equations were prospectively applied, better agreement with the thermodilution cardiac index was obtained by pulsed wave Doppler directly from mean velocity (SD 240 ml/min per m^2) than when aortic annular area was considered in the calculation (SD 428 ml/min per m^2). Similar results were obtained by continuous wave Doppler (SD 433 vs. 599 ml/min per m^2) but with less accuracy.**

Conclusions. **Left ventricular outflow tract mean velocity determined by pulsed wave Doppler permits easy, accurate cardiac index quantification in the absence of left ventricular outflow abnormalities. The simplicity of this method enhances its clinical applicability in noninvasive monitoring of cardiac index.**

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Quantification of cardiac index, a fundamental variable of cardiovascular function, is necessary for adequate prognostic evaluation and proper patient management in diverse clinical situations. To date, only invasive methods have been generally accepted for cardiac index measurement and their use limited to catheterization laboratories and intensive care units. However, in the past decade, Doppler echocardiography has been proposed for noninvasive quantification of cardiac output (1–8). Cardiac output has been calculated (9) as the product of the Doppler flow mean velocity and cross-sectional area at various points in the heart and great vessels, with the left ventricular outflow tract one of the most frequently used sites (10–12). Nevertheless, the clinical application of Doppler echocardiography for measurement of cardiac index is far from widespread, due principally to the diversity of methods used and the conflicting results reported.

Several studies have identified measurement of cross-sectional area by echocardiography as the main source of error in flow volume quantification (4–8,12–15), and attempts have been made to relate Doppler velocity values to cardiac output and stroke volume, albeit with poor results (16–18). However, the relation between mean velocity and cardiac index has not been investigated.

The aim of this study was to ascertain whether cardiac index can be directly derived from left ventricular outflow and aortic mean velocity in the absence of left ventricular outflow abnormalities.

Methods

The study included three phases: In *phase I*, the normal ratio of left and right ventricular outflow tract mean velocity

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was defined in a series of normal subjects to establish objective criteria for excluding patients with left ventricular outflow abnormalities not detected by Doppler echocardiographic study, and the reproducibility of variables used to calculate aortic flow volume was analyzed. In *phase II*, cardiac index by Doppler echocardiography using the conventional method (Mean velocity × Area index × 60) and mean velocity were correlated with the thermodilution cardiac index, and regression equations were derived. In *phase III*, the accuracy of these equations was prospectively evaluated.

Study patients. Three hundred six patients were studied by Doppler echocardiography.

Phase I. The study group comprised consecutive patients referred for preoperative assessment from the ophthalmology and orthopedic departments. Inclusion criteria were 1) absence of history or symptoms suggestive of cardiovascular, respiratory, renal or systemic disease; 2) normal physical examination results, including normal blood pressure; and 3) normal findings on electrocardiographic, chest X-ray film, routine blood test and Doppler echocardiographic study. Exclusion criteria were 1) presence of known risk factors for coronary artery disease; 2) pathologic obesity; and 3) recent illness. The initial study group included 170 patients. In all patients, normal values of Doppler left and right ventricular outflow mean velocity were assessed. In 14 patients, right ventricular outflow velocity was not correctly defined and they were excluded. Accordingly, the final study group comprised 156 patients (84 men, 72 women; mean [±SD] age 37 ± 20 years, range 6 to 86). Reproducibility of left ventricular outflow tract and aortic mean velocity determined by pulsed and continuous wave Doppler, respectively, and aortic annular area measured by cross-sectional echocardiography were studied in 20 patients (14 men, 6 women; mean age 42 ± 12 years, range 21 to 62).

Phase II. We studied 66 consecutive patients in the intensive care unit who were undergoing pulmonary artery catheterization and who fulfilled the following criteria: presence of sinus rhythm and absence of left ventricular outflow tract abnormalities. Six patients with abnormal left/right ventricular outflow tract mean velocity ratio, as defined in phase I, were excluded. Thus, the study group included 60 patients (38 men, 22 women; mean age 51 ± 15 years, range 22 to 73) with acute myocardial infarction (n = 32), severe congestive heart failure (n = 13), operation (n = 11) and sepsis (n = 6).

Phase III. Seventy consecutive patients in the intensive care unit who were in sinus rhythm and had an implanted Swan-Ganz thermodilution catheter were studied. Eight patients with an abnormal left/right ventricular outflow tract mean velocity ratio were excluded. Thus, 62 patients (45 men, 17 women; mean age 54 ± 17 years, range 27 to 78) were studied, including 29 with acute myocardial infarction, 17 with severe heart failure, 13 with operation and 3 with sepsis.

Doppler echocardiographic studies. *Phase I.* A Vingmed CFM 700 or Hewlett-Packard Sonos 500 apparatus equipped with 2.25- and 3.5-MHz mechanical transducers was used. A 2.25-MHz split-crystal stand-alone angulated (Pedof) transducer was used for continuous wave Doppler studies. Aortic annular diameter, obtained by cross-sectional echocardiography in the parasternal long-axis view, was measured from the trailing edge of the anterior echo to the leading edge of the posterior echo at the attachment of the aortic leaflets at the time of maximal aortic valve opening in early systole. Aortic annular area was calculated according to the following formula: $\pi \times (D/2)^2$, where D = diameter averaged in three cardiac cycles. Aortic annular area index was calculated as the ratio of aortic annular area to body surface area.

Left ventricular outflow tract velocity was studied by pulsed wave Doppler and aortic flow velocity by continuous wave Doppler from the apical window. For pulsed wave Doppler studies, the sample volume was positioned at the center of the left ventricular outflow tract, just proximal to the start of valvular flow acceleration, usually 0.5 cm below the aortic valve leaflets (13). Every effort was made to record the highest velocity tracing with the least spectral dispersion. Right ventricular outflow tract velocity was studied from the short-axis view with the sample volume placed 0.5 cm proximal to the pulmonary valve, as on the left side.

All measurements were performed directly from the screen using built-in calipers and roller ball. Continuous wave recordings were measured after the maximal envelope of the velocity tracing and pulsed Doppler recordings were digitalized following the contour of the darkest portion of the spectral display (modal velocity). Mean velocity of a single cardiac cycle was obtained by tracing the velocity curve continuously throughout the cardiac cycle. Diastolic flow was assumed to be null, and only systolic flow was considered in the mean velocity calculation. Five cardiac cycles were averaged for each measurement.

Reproducibility of the aortic annular area determined by two-dimensional echocardiography and mean velocity quantified by pulsed and continuous wave Doppler were studied. Two observers conducted two studies on two consecutive days. Neither observer was informed of the results of the other evaluations.

Phase II. Doppler echocardiographic study was performed immediately before thermodilution cardiac index quantification. Cardiac index was calculated by the conventional method from mean velocity determined by pulsed and continuous wave Doppler and aortic annular area index, according to the following equation:

$$CI = MV \times 60 \times AA/BSA,$$

where CI = cardiac index; MV = mean velocity; AA = aortic annular area; and BSA = body surface area.

Cardiac index determined by Doppler echocardiography using conventional method and mean velocity was correlated with the thermodilution cardiac index, and regression equations were derived.

Phase III. The protocol was the same as that used in phase II. Cardiac index was quantified by conventional method, directly from mean velocity, using the regression equations defined in phase II.

Table 1. Mean Values of Aortic Annular Area Index and Mean Velocity of Flows Determined by Doppler Echocardiography

	Mean ± SD	Coeff of Variation (%)	Normal Range
AA/BSA (cm^2/m^2)	2.1 ± 0.2	11	1.7–2.5
LVOT MV (cm/s)	19.5 ± 3.4	18	13.2–25.8
RVOT MV (cm/s)	18.2 ± 3.8	21	11.0–25.4
AMV (cm/s)	27.2 ± 4.7*	20	18.3–36.1
LVOT/RVOT MV	1.1 ± 0.1	10	0.9–1.3

*Aortic mean velocity (AMV) was significantly higher than left and right ventricular outflow tract mean velocities (LVOT MV and RVOT MV, respectively, $p < 0.01$). AA/BSA = aortic annular area index; Coeff = coefficient.

Thermodilution studies. Cardiac index was measured by the thermodilution method immediately after completion of the echocardiographic study. Cardiac output was obtained with a Waters TC-2 computer by rapidly injecting 10 ml of 0.9% cold sodium chloride solution through the proximal part of the Swan-Ganz catheter. Thermodilution curves were recorded, and those showing irregularities or lacking a clear early peak were considered inadequate and rejected. Cardiac output was computed as the average of three consecutive adequate measurement values differing <10%. If the difference between the lowest and highest values of the three measurements was >10%, two additional cardiac output measurements were performed, and the extreme values discarded. The physician performing the thermodilution studies was unaware of the results of the Doppler study.

Statistical analysis. Results are presented as mean value ± SD. The relation between continuous variables was tested by linear regression analysis. The standard error of the estimate was calculated. To evaluate the scatter between Doppler and thermodilution measurements of cardiac index, values were examined by the Bland and Altman method (19). Systematic differences among methods were tested by the Student *t* test; $p < 0.05$ was considered statistically significant. In the reproducibility study, the intraclass coefficient of correlation was calculated (20). Variability of paired measurements was obtained as the difference between measures expressed as a percent of the mean value of the pair.

Results

Phase I. Normal values and reproducibility analysis. Normal values of aortic annular area index and Doppler mean velocity of flows studied are shown in Table 1. Correlation between left and right ventricular outflow tract mean velocity determined by pulsed wave Doppler was good ($r = 0.83$, $p < 0.0001$). Measurement of aortic annular area by two-dimensional echocardiography had a large intraobserver and interobserver variability (13.1 ± 6% and 14.7 ± 7.4%, respectively). Left ventricular outflow tract mean velocity by pulsed wave Doppler presented much lower intraobserver (5.1 ± 4.3%) and interobserver (6.3 ± 4.8%) variability than aortic mean velocity by continuous wave Doppler (9.3 ± 5.7% and 10.5 ± 9.4%, respectively).

Intraclass correlation coefficient $\hat{R}$ was higher, indicating better reproducibility for left ventricular outflow tract mean velocity obtained with pulsed wave Doppler ($\hat{R} = 0.83$, $p < 0.0001$) than aortic mean velocity with continuous wave Doppler ($\hat{R} = 0.79$, $p < 0.0001$). Measurements of aortic annular area by echocardiography showed lower reproducibility ($\hat{R} = 0.74$, $p < 0.001$).

Phase II. Doppler echocardiography versus thermodilution cardiac index. Cardiac index (CI) quantified by thermodilution (TD) (range 1,100 to 5,400 ml/min per m^2) and by Doppler echocardiography using the conventional method showed acceptable correlations when pulsed (PWD) or continuous wave Doppler (CWD) was used:

$$r = 0.90, \quad CI_{TD} = 1.20\, CI_{PWD} + 357; \qquad [1]$$

$$r = 0.86, \quad CI_{TD} = 0.91\, CI_{CWD} + 262, \qquad [2]$$

$p < 0.001$, respectively (Fig. 1). A systematic underestimation was obtained (mean value of differences −856 ± 525 ml/min per m^2 [−28 ± 13%], $p < 0.01$) by pulsed wave Doppler. By continuous wave Doppler, no systematic overestimation or underestimation resulted (mean difference 84 ± 626 ml/min per m^2 [4 ± 18%]).

Left ventricular outflow tract mean velocity and aortic mean velocity determined by pulsed and continuous wave Doppler, respectively, had excellent correlation with thermodilution cardiac index:

$$r = 0.97, \quad CI_{TD} = 172\, MV_{PWD} - 172; \qquad [3]$$

$$r = 0.93, \quad CI_{TD} = 129\, MV_{CWD} - 255, \qquad [4]$$

$p < 0.001$, respectively (Fig. 2).

Phase III. Comparison between cardiac index values determined by Doppler echocardiography and thermodilution. Thermodilution cardiac index ranged from 1,500 to 6,400 ml/min per m^2. When the conventional method was used to calculate cardiac index, using the regression equations 1 and 2, agreement with thermodilution was weak (Table 2, Fig. 3).

Better results were obtained when cardiac index was derived directly from mean velocity. The best agreement was given by left ventricular outflow mean velocity by pulsed wave Doppler using regression equation 3. Less accuracy was obtained from aortic mean velocity derived by continuous wave Doppler using the equation 4 (Table 2, Fig. 4).

Discussion

This study demonstrates that left ventricular outflow tract mean velocity determined by pulsed wave Doppler provides a simple, reliable noninvasive estimation of cardiac index in patients without left ventricular outflow tract abnormalities. Measurement of aortic annular area by two-dimensional echocardiography has low reproducibility, and inclusion of this area in the calculation of cardiac index does not improve accuracy of the estimation.

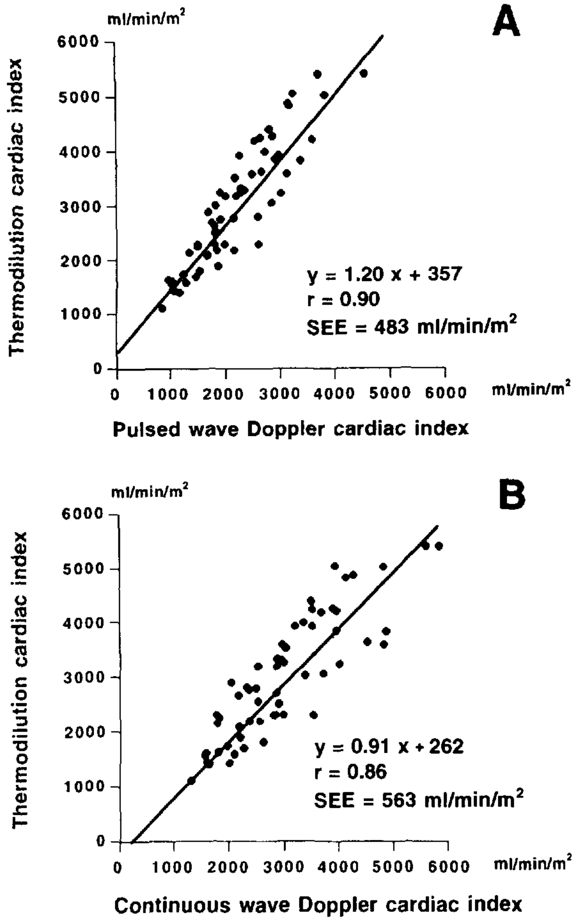

Figure 1. Correlation between cardiac index determined by thermodilution technique and by Doppler echocardiography using the conventional method (Cardiac index = Mean velocity × 60 × Aortic annular area index). The standard method (thermodilution cardiac index) is the variable to be predicted in phase III of this study; for this reason it is displayed on the **y axis**. Mean velocity was derived by pulsed (**A**) and continuous (**B**) wave Doppler.

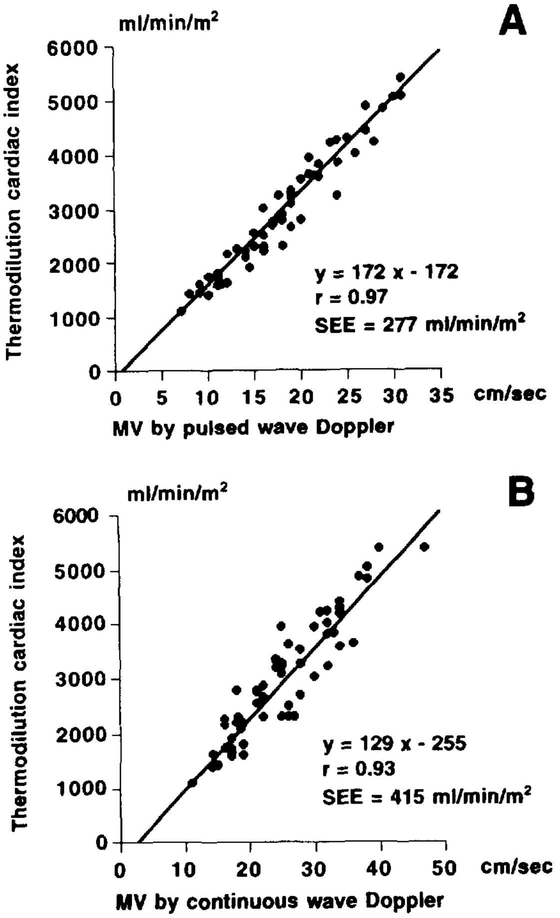

Figure 2. Correlation between cardiac index, determined by the thermodilution technique, and left ventricular outflow tract mean velocity (MV), determined by pulsed wave Doppler (**A**), and aortic mean velocity, derived by continuous wave Doppler (**B**). Thermodilution cardiac index is displayed on the **y axis** as in Figure 1.

Flow, velocity and area. Multiple methods have been described for quantification of cardiac output from the product of Doppler-derived blood flow velocity and cross-sectional area at different circulation sites (1–15). In adult patients, aortic flow analysis from the apical view has been shown to yield the best results (10–15). Experimental studies (21–23) have proved that Doppler ultrasound permits accurate measurement of blood flow velocity. However, most studies (4–8,12,14) have considered measurement of echocardiographic cross-sectional area at the site of flow detection to be the main source of error in cardiac output quantification. To avoid this limitation, some investigators (24,26) have suggested assessing flow volume from Doppler velocity only, defining the terms of stroke distance and minute distance. Different studies have related velocity-time integral values to cardiac output or stroke volume (16–18) with poor results, leading to the conclusion that measurement of the cross-sectional area is necessary for cardiac output quantification (26–28). A possible explanation for these results is that, whereas flow velocity is independent of body surface area (29), cardiac output and stroke volume are affected by it. Our results demonstrate good relation between mean velocity (cm/s) and cardiac index (cm^3/s per cm^2), variables expressed in velocity units and independent of body surface area. Similarly, velocity-time integral values (cm) must be related to the stroke volume index (cm^3/cm^2), both expressed in units of distance. In addition, aortic annulus and left ventricular outflow tract dimensions are closely related to body

Table 2. Differences Between Cardiac Index Values Determined by Doppler Echocardiography and Thermodilution

	Mean (±SD) Difference (%)
Conventional method	
LVOT MV (ml/min per m^2)	23 ± 428 (1 ± 13)
AMV (ml/min per m^2)	72 ± 599 (1 ± 17)
MV method	
LVOT MV (ml/min per m^2)	−18 ± 240 (−1 ± 7)
AMV (ml/min per m^2)	19 ± 433 (1 ± 13)

Abbreviations as in Table 1.

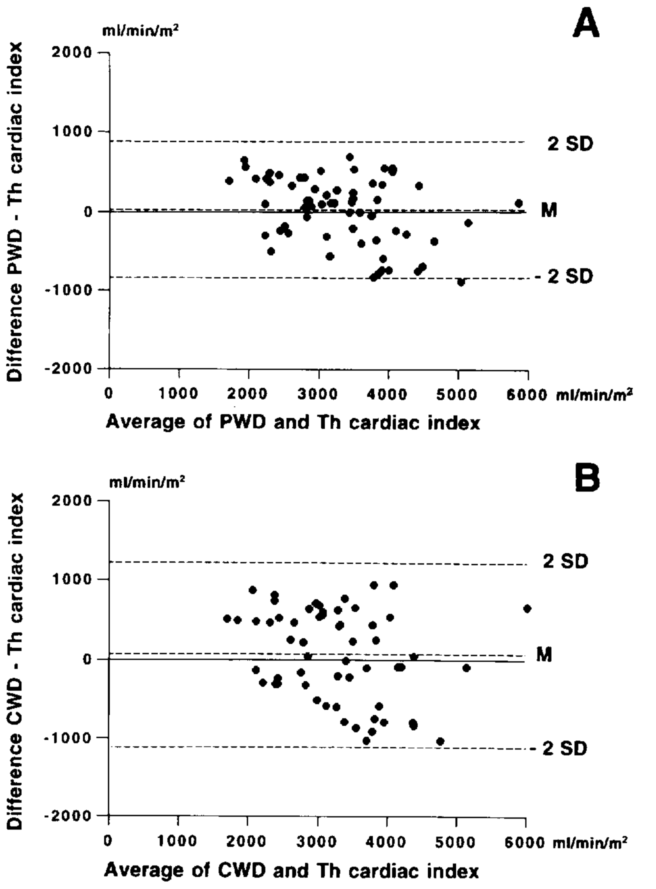

Figure 3. Agreement between cardiac index derived by Doppler echocardiography using the conventional method and thermodilution (Th). Cardiac index (CI) was quantified (**A**) by pulsed wave Doppler (PWD) by the equation CI = 1.20 CI_{PWD} + 357 and (**B**) by continuous wave Doppler (CWD) by the equation CI = 0.91_{CWD} + 262. **Middle line** (M) = mean difference between methods; **two outer lines** = 95% confidence intervals for differences between methods.

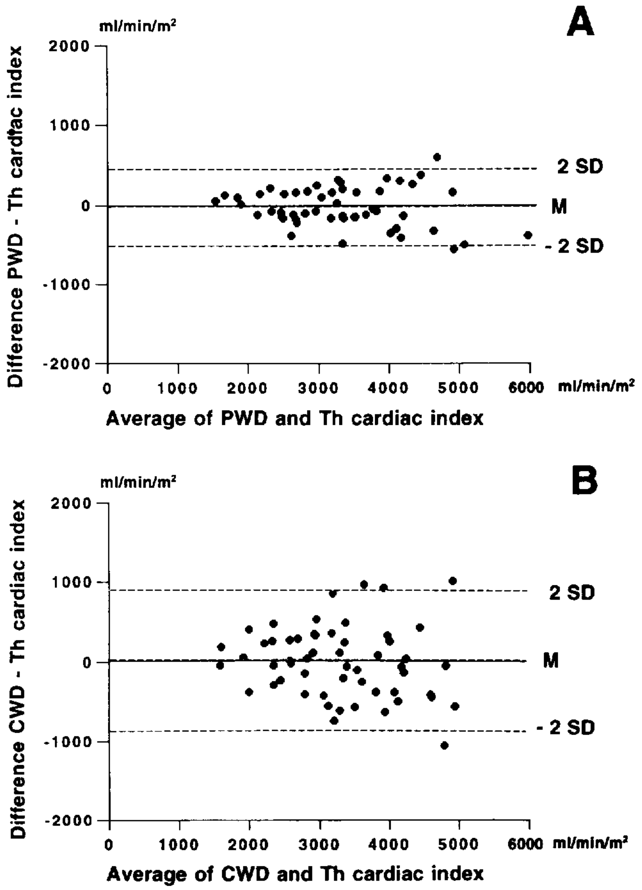

Figure 4. Agreement between cardiac index derived directly from mean velocity and thermodilution (Th). Cardiac index (CI) was quantified from left ventricular outflow tract mean velocity (MV) determined by (**A**) pulsed wave Doppler (PWD) by the equation CI = 172 MV_{PWD} − 172 and (**B**) from aortic mean velocity by continuous wave Doppler by the equation CI = 129 MV_{CWD} − 255. **Middle line** (M) = mean difference between methods; **two outer lines** = 95% confidence intervals for differences between methods.

surface area in patients without left ventricular outflow abnormalities (30–34). Therefore, it would appear more advisable to calculate cardiac index directly from mean velocity than to multiply this value by the echocardiographic cross-sectional area and then divide it by body surface area.

Continuous versus pulsed wave Doppler. We observed no systematic error in cardiac index quantification when aortic annular index measured by echocardiography and aortic mean velocity determined by continuous wave Doppler were considered. However, a significant underestimation of cardiac index resulted from left ventricular outflow tract mean velocity derived by pulsed wave Doppler and aortic annular index values. Other studies have reported similar results (15,27,35,36), which has led to measurement of aortic annular area by the leading-edge method (4,15,37). It is possible that underestimation of cardiac index by pulsed wave Doppler occurs because the product of left ventricular outflow tract mean velocity and aortic annular area, which is smaller than the left ventricular outflow tract area, results in systematic error.

Left ventricular outflow tract mean velocity determined by pulsed wave Doppler correlated better with thermodilution cardiac index than aortic mean velocity derived by continuous wave Doppler and showed better reproducibility. These results could be related to the instability of the aortic vena contracta and aortic valve area variations secondary to stroke volume changes (34). However, in the left ventricular outflow tract, flow is more stable and has a flat profile (38), and dimensions remain constant during more widely varying hemodynamic conditions (34).

Study limitations. This study has several limitations. First, thermodilution is not an ideal reference standard for new cardiac index quantification methods (39). Nevertheless, careful determination of cardiac index by the thermodilution technique proved to have an accuracy similar to widely accepted standard methods (40,41) and is the technique most used in clinical practice.

Second, aortic regurgitation and left ventricular outflow tract abnormalities prevent direct quantification of cardiac index from Doppler-derived left ventricular mean velocity.

However, conventional Doppler echocardiographic methods, which include cross-sectional area determination, present the same limitation (28). In addition, cardiac disease that affects left ventricular outflow dimensions, such as left ventricular hypertrophy or dilated cardiomyopathy, represents a theoretic limitation for quantifying cardiac index directly from mean velocity. In hypertrophied ventricles, outflow tract dimensions are frequently smaller for given body surface area. Therefore, it would be advisable to verify normality of the left/right ventricular outflow tract mean velocity ratio before cardiac index calculation as performed in the present study. In severe dilated cardiomyopathies with significant outflow dilation of both ventricles, mean velocity could underestimate cardiac index; therefore, measurement of the left ventricular outflow area is advisable.

Conclusions. Doppler-derived left ventricular outflow mean velocity is directly related to cardiac index in the absence of left ventricular outflow tract abnormalities. Measurement of the cross-sectional area of the aortic annulus by two-dimensional echocardiography for cardiac index calculation does not improve results obtained directly from Doppler mean velocity.

Cardiac index quantification directly from Doppler mean velocity is simple, accurate and practical and should enhance the clinical value of Doppler echocardiography for providing noninvasive measurement and monitoring of this important variable of cardiovascular function.

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